REMARKS

Claims 1-4, 5-6, 10-11, 57-59 and 60-61 are under examination. The specification has been amended to correct informalities. No new matter has been added. Reconsideration is requested.

The Examiner indicated that the priority statement was improperly located in the specification. Amendment has been made to place the statement at the beginning of the specification.

The Examiner indicated that the references in the Search Report will not be listed on any issued patent unless provided on a separate listing. A PTO SB/08A is filed herewith. It is not believed that any fee is due as the references contained thereon are already of record.

The Examiner appears to have reversed her position on the amendment to the drawings. In accordance with her suggestion, a copy of the originally filed drawings is attached hereto for entry into the application. The figure legends on page 12 and 15 have been amended as the Examiner suggested.

The disclosure has been objected to because the primer sequences on page 40 do not have SEQ ID NOs. The specification has been amended to insert SEQ ID NOs. Withdrawal of the rejection is respectfully requested.

The disclosure was objected to because it contained an embedded hyperlink and/or other form of browser-executable code. The specification has been amended to remove the executable code.

Claims 1-4, 10-11 and 57-59 have been rejected under 35 USC § 112, first paragraph, because the specification, while being considered by the Examiner to be enabling for an isolated human alpha-synuclein mutated to adenine at position 209, does not reasonably provide enablement for any mutated human alpha-synuclein or homolog thereof of any other mutation at position 209. This rejection is traversed for the following reasons.

First, it is respectfully submitted that there are only a limited number of possible mutations at position 209, and thus a limited number of mutations to be made and used. This is easily within the skill of an ordinary artisan, and would not require undue experimentation. Accordingly, it is submitted that claims 4 and 59 are clearly enabled.

Reconsideration and withdrawal of the rejection with respect to claims 4 and 59 is accordingly requested.

Second, it is respectfully submitted that persons of skill in the art will be able, using the methods described in the specification and the general knowledge of the art, to make and use the nucleic acids of claims 1-3, without undue experimentation.

Two articles subsequent to the present disclosure demonstrate that OTHER missense mutations in the alpha-synuclein gene can cause Parkinson's disease.

They are:

Kruger et al. Ala30Pro mutation in the gene encoding alpha-synuclein in Parkinson's disease. Nature Genetics, 18:106-108, 1998.

Zarranz et al. The New Mutation, E36K, of alpha-synuclein causes Parkinson and Lewy Body Dementia. Ann Neurol 55:164-173, 2004.

Copies are enclosed for the Examiner's information. It is respectfully submitted that this provides evidence that other such mutations can be made and used without undue experimentation.

It is further submitted that claims 10-11 and 57-58 can be carried out without undue experimentation given possession of the nucleic acids of claims 1-3, and are therefore enabled. Reconsideration and withdrawal of the rejection with respect to claims 1-3, 10-11 and 57-58 is respectfully requested.

Claims 1-4, 10-11 and 57-59 have been rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. This rejection is traversed for the following reasons.

It is the Examiner's position that the genus disclosed by applicants encompasses nucleotide sequences that are at least 25% homologous to SEQ ID NO:1 and alpha synuclein sequences wherein the mutation is a substitution deletion, transversion or transition, and that the description at pages 26 and 30 of the specification is insufficient to provide support for the scope of the claimed subject matter.

First, with respect to claims 4 and 59, it is respectfully submitted that the description provided in the specification is clearly adequate to cover the limited number of variants containing a mutation at position 209. Such variants can be easily made and tested given the level of knowledge in the art and the teachings of the present

specification. Accordingly, reconsideration and withdrawal of the rejection of claims 4 and 59 are respectfully requested.

Furthermore, as noted above, two articles subsequent to the present disclosure demonstrate that OTHER missense mutations in the alpha-synuclein gene can cause Parkinson's disease. It is respectfully submitted that this provides ample evidence that persons of skill in the art would be able to practice the invention as claimed in claims 1-3, 10-11 and 57-58.

Accordingly, it is respectfully submitted that the presently claimed invention meets both the written description and the enablement requirements for patentability. Reconsideration and withdrawal of the rejections are respectfully requested.

Claims 1-3 and 57-58 were rejected under 35 USC § 102(a) as being anticipated by Xia et al. Annals of Neurology: 40:207-215 (1996). It is the Examiner's position that Xia et al. teach an isolated synuclein nucleic acid comprising a polymorphism. This rejection is traversed for the following reasons.

The article by Xia et al. describes a dinucleotide polymorphism, the NACP-Rep1 repeat, that is located 11,000 basepairs UPSTREAM of the start of transcription of the alpha-synuclein gene. It is NOT in the coding region and does NOT produce a change in the protein that is encoded by the alpha-synuclein gene. The present claims are for missense mutations that alter the structure of the alpha-synuclein, resulting in Parkinson's disease. Accordingly, it is respectfully submitted that the Xia reference does not anticipate Claims 1-3 and 57-58. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 10 and 11 were rejected under 35 USC § 103(a) as being unpatentable over Xia et al. It is the Examiner's position that Xia et al. teach an isolated synuclein nucleic acid comprising a polymorphism, and that it would have been obvious to one of skill in the art to take the sequence taught by Xia et al. and use it to make a recombinant vector and transform cells with the vector for either replication purposes or protein expression purposes. This rejection is respectfully traversed.

As noted above, the Xia reference describes a dinucleotide polymorphism that is located 11,000 basepairs UPSTREAM from the start of the transcription of the alpha-synuclein gene. Accordingly, it is respectfully submitted that there is no way this

polymorphism could suggest the invention as claimed in claims 10 and 11. Reconsideration and withdrawal of the rejection are respectfully requested.

Applicants appreciate the Examiner's indication that claims 5, 6 and 60-61 would be allowable if rewritten in independent form to include all the limitations of the base claim and any intervening claims. Applicants defer rewriting these claims in independent form until the Examiner has an opportunity to consider the present amendments and arguments.

Should any additional fee be required, please charge the same to Deposit Account No. 22-0261 and notify applicants' attorney.

Respectfully submitted,

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